

Improved Monovalent Ion-Carboxylate Interactions in the Drude Polarizable Force Field using QM and MD Calculations

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Explicit atomistic polarizability is crucial to the accurate description of interactions between monovalent ions and carboxylate groups, such as ASP and GLU amino acids. The CHARMM Drude polarizable force field (FF) models polarizability by adding charged particles with a small mass to the non-hydrogen atoms. In the Drude FF the parameters for ions were optimized by targeting hydration free energies supplemented with quantum mechanical (QM) interactions with water. However, the interactions between the different ions involved in salt bridges were not considered. Here we present a new set of pair-specific Lennard-Jones (LJ) r_{\min} parameters and electrostatic damping factors, implemented via a Thole screening function, between each of Li⁺, Na⁺, and K⁺ ions and the carboxylate oxygen atom type. We fitted the parameters using a combined approach utilizing different types of reference data. The first approach uses various QM interaction energies between the monoatomic ions and acetate in gas phase as references, with the goal of fitting Drude interaction energies of the same conformations. The second approach is to run molecular dynamics (MD) simulations of salt solutions comprised of the monoatomic ions and acetate for several parameter sets, and comparing the resulting osmotic pressures directly to available experimental data. We computed single point QM interaction energies of ion-acetate complexes, varying the ion position linearly along three specific directions with respect to one of the C-O bonds. We then used novel scoring criteria to fit the Drude interaction energies to these QM references. The parameter optimization was performed using a global search over a range of LJ r_{\min} values as well as a range of Thole damping factors. To calculate osmotic pressure, we setup simulations of the salt solutions with a simulated semi-permeable membrane, which exerted a restraining force only on the ions and not on water. The osmotic pressure could then be calculated as a trajectory average of the forces exerted by the semi-permeable membrane. The gas-phase QM fitting produced a selection of parameter sets, some of which yielded osmotic pressures in agreement with the experimental data. Thus, we were able to select parameters which fitted both gas-phase QM data and condensed phase osmotic pressure data reasonably well. Notably, the scoring criteria used is focused on the local shape of the minima of both the QM and Drude energy surfaces, rather than absolute differences in the full interaction energy surface. This implies that careful criteria selection in parametrization problems is crucial, especially when exact reproduction of QM energy surfaces is impossible and when considering transferability of gas-phase derived parameters to condensed phase.